IN THE CIRCUIT COURT OF
GREENBRIER COUNTY, WEST VIRGINIA

STATE OF WEST VIRGINIA

VS.

MARY BETH DAVIS

CRIMINAL ACTION
NO. 96-F-102

AFFIDAVIT

I, Michael A. Evans, state as follows:

A. Professional Experience & Education

I am a toxicologist employed by AIT Laboratories in Indianapolis, Indiana. I have been employed in this position since March 1990. I received my Bachelor's of Science Degree with majors in Biology and Chemistry from St. Joseph College, Rensselaer, Indiana in 1967. I received my Doctorate Degree in Toxicology from Indiana University in 1974. I was certified as a Diplomat by the American Board of Toxicology in 1981 and I have been recertified by the same Board in 1986 and 1991. I have served as a toxicologist on legal matters for over 15 years. I was a member of the faculty at the University of Illinois College of Medicine from 1976 until 1987. I served as tenured Professor of Toxicology, Director of the Graduate Program In Toxicology, and Director of the State Department of Toxicology at Indiana University School of Medicine from 1987 until 1989. I have over 100 scientific publications and have served as a consultant to the following international, Federal, and State agencies: World Health Organization, The World Bank, US Food and Drug Administration, US Environmental Protection Agency, US National Institute of Health, US Department

of Transportation, US Drug Enforcement Agency (DEA), Indiana Controlled Substances Licensing Board and the Indiana Governor's Task Force to Reduce Drunk Driving. My work in legal settings has involved the preparations of affidavits, written reports, and testimonies as an expert toxicologist in criminal and civil court cases, employee arbitration's hearings, workman's compensation hearings, and post-conviction relief hearings.

Since 1980 I have worked on over 200 cases on which I have conducted extensive toxicological reports and as assisted prosecutors and attorneys in preparing for court cases and hearings. These cases and hearings have been in federal court, military proceedings as well as State Courts. I have served as an expert toxicologist in Federal Courts and in over 30 State Courts including Indiana, Illinois, Kentucky, Michigan, Pennsylvania, South Dakota, Virginia, Vermont, California, Colorado, Texas, Arkansas, Ohio, Montana, Mississippi and Florida.

In my over 20 years in academic medicine I have conducted extensive research and provided extensive education in the science of Pharmacology & Toxicology at the following: Vanderbilt University, University of Illinois Health Science Center, Illinois Institute of Technology, US Occupational Safety and Health Agency National Training Center, Sichuan Institute of Traditional Chinese Medicine (People's Republic of China) and Indiana University. In addition, I have provided lectures and courses in toxicology as an invited speaker in the following countries India, Italy, Israel, China, South America (Peru) and Scotland.

The following information is offered in particular interest to this report:

1. Developed, directed and taught a Pediatric Pharmacology Program for the University of Illinois School of Medicine. This Program was used as part of the Core Educational Program for Medical Students at the University of Illinois.

2. Chaired an International Symposium on Pediatric Pharmacology at the 1985 International Congress on Pharmacology, Invited speakers to the Program included key scientist in Pediatric Pharmacology & Toxicology at the US National Iinstitute of Health, the US Food & Drug Administration, and the US National Institute of Child Health & Development.

3. Invited speaker at several US Programs in Pediatric & Neonatology Board Certification Programs on the topics of Drug Disposition & Drug Toxicity.

4. Conducted & published original research in Pediatric Pharmacology & Toxicology

5. Served as a Principal Scientist in the development & clinical application of Indomethacin for treatment of cardiac defects in newborn infants. This research led to the elimination of surgical intervention for these cardiac defects.

6. Developed, directed and taught the Graduate Program in Toxicology at the University of Illinois Health Science Center (Chicago).

7. Developed, directed and taught the Graduate Program in Toxicology at the Illinois Institute of Technology (Chicago).

8. Directed and taught the Graduate Program in Toxicology for Indiana University.

9. Have lectured to Medical Students, Graduate Students and Physicians on the topics of Pediatric

Pharmacology & Toxicology at the following educational institutions:

- Vanderbilt University School of Medicine
- University of Illinois School of Medicine – Chicago
- University of Illinois School of Medicine – Rockford
- University of California – Berkley
- Indiana University School of Medicine
- Cook County Graduate School of Medicine
- University of Illinois School of Public Health

10. Served as Director of the Indiana State Department of Toxicology (Indiana State Toxicologist).

11. Served as Faculty Member and Co-investigator of the first Federally Funded National Research Center on Alcohol and Alcoholism.

12. Serve as a Certified inspector and Team Leader for the College of American Pathologists (CAP) in Inspection of Hospital and Private laboratories.

13. Serve as Certified Inspector for the SAMHSA (Formerly NIDA, US Department of Health and Human Services) Laboratory Certification Program

14. Founded and currently direct, as President & CEO and as Director of Laboratories, AIT Laboratories, Inc. which serves as the laboratory of choice to the largest consortium of Hospitals in Indiana for monitoring of Blood Caffeine in newborns

15. Founded and currently direct, as President & CEO and as Director of Laboratories, AIT Laboratories, Inc. which serves as the laboratory of

choice to the Indiana State Department of Health for Newborn Drug Testing

16. Invited speaker and participant on a Pan-American Symposium on Cocaine sponsored by the US State Department and the National Institute on Drug Abuse

17. Invited Speaker and Lecturer to Graduate Students, Medical Students, Physicians (Post-Graduate Education Programs), Federal Laboratory Inspection Programs, State and Local Law Enforcement Officers and Federal OSHA inspectors (OSHA Training Institute) an the following topics:

    - Toxicology of Drugs (Sources, Disposition and Toxicity)
    - Drug Disposition: Includes the processes by which drugs & chemicals are absorbed, distributed and eliminated from the body. A particular interest in my lectures was Drug Distribution in the Fetal, Newborn & Pediatric Patient
    - Toxicology of Stimulants including Caffeine, Amphetamines & Cocaine
    - Laboratory Procedures: includes Specimen Chain of Custody Procedures, Specimen Transport and Specimen Storage Procedures

18. Assisted in the development and operations of the United States Navy Urine Drug Testing Program.

19. Assisted in the development and implementation of the Federal Guidelines for the Federal Government Urine Drug Testing Program (Which includes the US Department of Transportation and Corporations governed by the US DOT)

20. Served as the Instructor of Quality Assurance/ Quality Control for Inspectors of the Federal Urine Drug Testing Program (Which includes the US Department of Transportation and Corporations governed by the US DOT)
21. Founded and currently direct, as President, AIT Laboratories which serves as the laboratory of choice for Law Enforcement & Criminal Justice agencies in more than 30 states.
22. Awarded multiple Research Grants by the National Institute of Health in the area of Pediatric Pharmacology & Toxicology
23. Organizer & Chairman of an International Symposium on the Pharmacology, Toxicology & the Abuse of Cocaine in our society. The International Symposium focused on the History of Cocaine in our culture, the basic biochemistry of Cocaine addiction and approaches to treatment of Cocaine toxicity & Cocaine addiction
24. Invited Speaker to the US State Department Pan American Conference on Cocaine

Attached to this document and designated as "Exhibit" is my curriculum vita reflecting my education, training, and experience in the science of toxicology.

B. Case Documents

The following items and documents have been provided for my review in the preparation of this report:

1. Letter dated 08/08/01 from R. Kevin Hanson to Dr. James Kraner
2. Toxicology Laboratory Report from Office of the Chief Medical Examiner for Lab Number 82-C-107

3. Litigation Package for Lab Number 82-C-107 to include:
    - Toxicology Request
    - Report of Medical Examiner Investigation
    - Chromatograms from Gas Chromatography Instruments (10 Total)
    - Spectrophotometric Spectroscopy Charts (2 Total)
    - Notes dated 3/22/82, 2:00 PM phone call with Dr. Hooper
    - Greenbriar Valley Hospital Discharge Summary Report for Tegan Davis (3 pages)
    - Laboratory Slips for Microbial Testing (4 Total)
    - SmithKline Clinical Laboratories Report for Tegan Davis
    - List of Drugs on Premise
    - Information on Dietac 12 hr. Capsules
4. Letter from Edward R. Friedlander, M.D. to Paul Detch dated 10/11/99
5. Letter from Jamese E. Heubi, M.D. to Paul Detch dated 10/16/99
6. Letter from Kevin E. Bove, M.D. to Paul Detch dated 12/05/99
7. Affidavit of Dr. Arthur Hupka
8. Deposition of Ronald C. Backer, M.D. dated 01/11/00

C. Specific information from the Case Documents

That based upon my training, experience and knowledge of toxicology as it relates to the effects and disposition of drugs of abuse, the following information was obtained from the Case Documents and considered for my opinions:

1. The concentrations of Caffeine reported in this case and comparison of those concentrations with the known and reported Caffeine concentrations from 14 cases of Caffeine lethality. The Table below provides a comparison (based on Percent) of the Caffeine Concentrations reported in this case with those reported from cases of Caffeine lethality.

Specimen	Tegan Davis Caffeine Conc.	Caffeine Lethality Mean Caffeine Conc.	Percent
Blood	66 ug/ml	183 ug/ml	36%
Brain	5.56 mg/kg	114 mg/kg	4.9%
Liver	9.04 mg/kg	241 mg/kg	3.6%
Kidney	11.06 mg/kg	184 mg/kg	6.0%

2. Deposition of Ronald C. Backer, M.D. dated 01/11/00 in which he states that the results of the Toxicology Report (as noted above for Caffeine) are correct.

D. Caffeine: Interpretation of Information

Caffeine, a central nervous system stimulant, is an odorless white crystalline powder or granule, with a bitter taste. It is sparingly soluble in water and ethanol at room temperature. The chemical name of caffeine is 3,7-dihydro-1,3,7-trimethyl-1 H-purine-2,6-dione. In the presence of citric acid it forms caffeine citrate salt in solution.

Mechanism of Action

Caffeine is structurally related to other methylxanthines, theophylline and theobromine. It is a bronchial smooth muscle relaxant, a CNS stimulant, a cardiac muscle stimulant and a diuretic. Although the mechanism of action of caffeine in apnea of prematurity is not known, several mechanisms have been hypothesized. These include: (1) stimulation of the respiratory center, (2) increased minute ventilation, (3) decreased threshold to hypercapnia, (4) increased response to hypercapnia, (5) increased skeletal muscle tone, (6) decreased diaphragmatic fatigue, (7) increased metabolic rate, and (8) increased oxygen consumption. Most of these effects have been attributed to antagonism of adenosine receptors, both A 1 and A 2 subtypes, by caffeine, which has been demonstrated in receptor binding assays and observed at concentrations approximating those achieved therapeutically.

Pharmacokinetics

Absorption

After oral administration of 10 mg caffeine base/kg to preterm neonates, the peak plasma level (C max) for caffeine ranged from 6-10 mg/L and the mean time to reach peak concentration (T max) ranged from 30 minutes to 2 hours. The T max was not affected by formula feeding. The absolute bioavailability; however, was not fully examined in preterm neonates.

Distribution

Caffeine is rapidly distributed into the brain. Caffeine levels in the cerebrospinal fluid of preterm neonates approximate their plasma levels. The mean volume of distribution of caffeine in infants (0.8-0.9 L/kg) is slightly higher than that in adults (0.6 L/kg). Plasma protein binding data are not available for neonates or

infants. In adults, the mean plasma protein binding in vitro is reported to be approximately 36%.

Metabolism

Hepatic cytochrome P450 1A2 (CYP1A2) is involved in caffeine biotransformation. Caffeine metabolism in preterm neonates is limited due to their immature hepatic enzyme systems. Interconversion between caffeine and theophylline has been reported in preterm neonates; caffeine levels are approximately 25% of theophylline levels after theophylline administration and approximately 3-8% of caffeine administered would be expected to convert to theophylline.

OVERDOSAGE

Following overdose, serum caffeine levels have ranged from approximately 50 mg/L to 350 mg/L. Signs and symptoms reported in the literature after caffeine overdose in preterm infants include fever, tachypnea, jitteriness, fine tremor of the extremities, hypertonia, opisthotonos, tonic-clonic movements, nonpurposeful jaw and lip movements, vomiting, hyperglycemia, elevated blood urea nitrogen, and elevated total leukocyte concentration. Seizures have also been reported in cases of overdose. One case of caffeine overdose complicated by development of intraventricular hemorrhage and long-term neurological sequelae has been reported. No deaths associated with caffeine overdose have been reported in preterm infants. In placebo-controlled clinical trials for newborns receiving Caffeine for prevention of apnea, caffeine blood levels ranged from 8 to 40 ug/ml.

F. Opinions

It is my opinion based upon reasonable scientific probability and based upon my training and experience and based upon the facts listed in the preceding paragraphs that:

1. The Chromatograms are consistent with and support the Toxicology Laboratory Report from Office of the Chief Medical Examiner for Lab Number 82-C-107
2. The information as contained in the Litigation package is inconsistent with and contrary to Caffeine as a cause of toxicity or death in this case.
3. The Blood and Tissue concentrations in this case indicate that:
   - The infant died before the Caffeine was distributed to the tissue (Brain, Liver, Kidney, etc.) from the Blood. Based on published Clinical studies of Caffeine, significant distribution for Caffeine from the Blood to the Tissues occurs within 10 minutes following intravenous administration and 30 minutes following oral administration.
   - The amount of Caffeine in the gastric contents (192 ug) is less than 1% of the Caffeine in a single cup of coffee. The average cup of coffee contains approximately 100 mg (or 100,000 ug) of Caffeine. As noted previously it requires 0.5 to 2.0 hours for total absorption (and peak Blood Concentrations) of Caffeine by oral administration.
   - The amount of Caffeine in the Liver (9.04 mg/kg) is less than 5% of the average Liver Caffeine Concentration in known cases of Fatal Caffeine Poisonings. The average Liver

concentration of Caffeine in known & reported Caffeine fatalities is 241 mg/kg.

- The amount of Caffeine in the Kidney (11.06 mg/kg) is less than 6% of the average Kidney Caffeine Concentration in known cases of Fatal Caffeine Poisonings. The average Kidney concentration of Caffeine in known & reported Caffeine fatalities is 184 mg/kg.
- The amount of Caffeine in the Brain (5.56 mg/kg) is less than 5% of the average Brain Caffeine Concentration in known cases of Fatal Caffeine Poisonings. The average Brain concentration of Caffeine in known & reported Caffeine fatalities is 114 mg/kg.
- The amount of Caffeine in the Blood (6.6 mg% or 66 ug/ml) is approximately 33% of the average Blood Caffeine Concentration in known cases of Fatal Caffeine Poisonings. The average Blood concentration of Caffeine in known & reported Caffeine fatalities is 183 ug/ml. However the reported Caffeine value of 183 ug/ml in Caffeine fatalities is for cases in which Caffeine has undergone distribution in the tissue. As documented by the Tissue Caffeine concentrations in this case, at the time of death Caffeine was not distributed to the tissue.

4. At the time of death there was minimal distribution of Caffeine throughout the body. Based on this minimal distribution of Caffeine at the time of death it is my opinion that death occurred within 5 to 10 minutes after Caffeine administration.

5. At the time of death there was minimal caffeine (less than 1% of the Caffeine in a cup of coffee) in the gastric contents and minimal distribution of

Caffeine to the tissues. Based on the known & reported oral & intravenous distribution times for Caffeine in humans, it is my opinion that the Caffeine in this case was administered by intravenous administration within 5 or 10 minutes prior to death.

6. The effects of Caffeine including toxicity and death are due to its pharmacological actions in the Central Nervous System (Brain). The effects of Caffeine in the Brain are concentration related (the higher concentration at the site of action, the greater the effect). In this case the Caffeine concentration in the Brain (5.56 mg/kg) was less than 5% of the average Brain Caffeine Concentration in known cases of Fatal Caffeine Poisonings. It is my opinion based on the above that the concentration of Caffeine in the Brain in this case was insufficient to produce either Caffeine toxicity or Caffeine death.

7. Plasma water (the fluid in the Blood) represents approximately 4.5% of the total weight of the body. Based on a body weight of 29 pounds the total Plasma water in this case is 1.3 Liters or 1300 ml (4.5% X 29 lbs.). The Blood Caffeine concentration in this case was 66 ug/ml. The total amount of Caffeine in the Blood in this case is therefore 66 ug/ml X 1300 ml or 85,800 ug or 85.8 mg. The average cup of coffee contains approximately 100 mg (or 100,000 ug) of Caffeine. The total amount of Caffeine in the Blood in this case is less than the amount of Caffeine in a single cup of coffee.

8. Since Caffeine in this case was only minimally (~ 5%) distributed to the tissues at the time of death it is my opinion that the total amount of Caffeine in the body (including the Blood with a

concentration of 66 ug/ml) is less than 200 mg or the amount of Caffeine in 2 cups of coffee.

9. The concentration of Caffeine in the Blood is only of importance as a relative measure of Caffeine at the site of action (i.e., the Brain). Caffeine does not have any relevant Pharmacological & Toxicological action in the Blood other than distribution to the organs. Since the Caffeine in this case had not been distributed to the Brain (The Brain Caffeine was less than 5% of the average Brain Caffeine Concentration in known cases of Fatal Caffeine Poisonings) the Blood Caffeine concentration of 66 ug/ml is of no Pharmacological & Toxicological significance.

10. I have reviewed the report of Dr. Art Hupka and find that his conclusions concerning Caffeine in this case are consistent with both the known & reported Pharmacology & Toxicology of Caffeine and the Laboratory Toxicology findings of this case. Specifically:

    - The amount of Caffeine in Tegan Davis at the time of death was equivalent to 1 to 1 & ½ cups of coffee (100 to 150 mg). This is consistent with my Opinion # 8
    - The amount of Caffeine in the Blood & Tissues (including Gastric Contents) of Tegan Davis is consistent with and supports the following opinions:
        - Caffeine was given by intravenous administration (Reference Opinions # 5)
        - Caffeine was administered within 15 minutes of death Reference Opinions # 4)
    - Caffeine is currently used as a Respiratory Stimulant in premature & newborn infants. In the 1970's Caffeine was also used as a

Treatment for overdose of CNS Depressant drugs. I note in the Medical Records of Greenbrier Valley Hospital (page 3) that "parenteral administration of Diazepam" was used to control symptoms. Diazepam (trade name is Valium) is a CNS Depressant drug.

FURTHER THE AFFIANT SAYETH NOT.

I AFFIRM UNDER THE PENALTIES FOR PERJURY THAT THE FOREGOING REPRESENTATIONS ARE TRUE.

DATED 5th DAY OF September, 2001.

/s/ [Illegible]
MICHAEL A. EVANS, Ph.D.

Subscribed and sworn before me /s/ Laura A. Portish.

a Notary Public, this 5th day of September, 2001.

SEAL:

/s/ Laura A. Portish
Laura A. Portish

My term expires: June 07, 2009

My County of Residence: Hendricks